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Lensless Imaging for Battlefield On-Chip Blood Diagnostics

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6. AUTHORS

Aydogan Ozcan, PhD

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAMES AND ADDRESSES

University of California - Los Angeles
Regents of the University of California, Los Angeles
Office of Contract and Grant Administration
Los Angeles, CA 90095 -1406

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13. SUPPLEMENTARY NOTES

The views, opinions and/or findings contained in this report are those of the author(s) and should not contrued as an official Department of the Army position, policy or decision, unless so designated by other documentation.

14. ABSTRACT

In this proposal timeline (1 Year total) we developed a new lensless on-chip imaging platform, termed LUCAS, to enable both diagnostic and sensing capabilities within a cost-effective hand-held unit that is specifically suitable for the battlefield settings. We established the proof of concepts of this imaging modality to achieve reliable and repeatable quantified whole blood analysis and compared our results against commercially available blood analyzers. Furthermore, we investigated the fundamental limits on the size of the detectable cell/bacteria with this

15. SUBJECT TERMS

lensfree imaging, blood analysis on a chip

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	15. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Aydogan Ozcan
UU	UU	UU	UU		19b. TELEPHONE NUMBER 310-500-6568

Report Title

Lensless Imaging for Battlefield On-Chip Blood Diagnostics

ABSTRACT

In this proposal timeline (1 Year total) we developed a new lensless on-chip imaging platform, termed LUCAS, to enable both diagnostic and sensing capabilities within a cost-effective hand-held unit that is specifically suitable for the battlefield settings. We established the proof of concepts of this imaging modality to achieve reliable and repeatable quantified whole blood analysis and compared our results against commercially available blood analyzers. Furthermore, we investigated the fundamental limits on the size of the detectable cell/bacteria with this platform. These accomplishments resulted in several refereed journal and conference articles. This research effort included one postdoctoral scholar as well as one graduate student working under the leadership of the PI.

List of papers submitted or published that acknowledge ARO support during this reporting period. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

1. H. Zhu, O. Yaglidere, T. Su, D. Tseng, and A. Ozcan, "Cost-effective and Compact Wide-field Fluorescent Imaging on a Cell-phone", Lab on a Chip, DOI:10.1039/C0LC00358A (2010)

2. T. Su, A. Erlinger, D. Tseng, and A. Ozcan, "A Compact and Light-weight Automated Semen Analysis Platform using Lensfree On-Chip Microscopy" Analytical Chemistry DOI:10.1021/ac101845q (2010)

3. O. Mudanyali, C. Oztoprak, D. Tseng, A. Erlinger, and A. Ozcan, "Detection of Waterborne Parasites using Field-portable and Cost-effective Lensfree Microscopy" Lab on a Chip, DOI:10.1039/c004829a (2010)
Selected as part of Emerging Investigators Special Issue: DOI: 10.1039/c0lc90044c

4. T. Su, S.O. Isikman, W. Bishara, D. Tseng, A. Erlinger and A. Ozcan, "Multi-angle lensless digital holography for depth resolved imaging on a chip" Optics Express Vol. 18, pp. 9690-9711 doi:10.1364/OE.18.009690 (2010)

5. A.F. Coskun, I. Sencan, T. Su, and A. Ozcan, "Lensfree wide-field fluorescent imaging on a chip using compressive decoding of sparse objects," Optics Express, Vol. 18, Issue 10, pp. 10510-10523 doi:10.1364/OE.18.010510 (2010)

6. S. Seo, S.O. Isikman, I. Sencan, O. Mudanyali, T. Su, W. Bishara, A. Erlinger, A. Ozcan, "High-throughput Lensfree Blood Analysis On a Chip," Analytical Chemistry DOI: 10.1021/ac1007915 (2010)

7. W. Bishara, T. Su, A.F. Coskun, and A. Ozcan, "Lensfree on-chip microscopy over a wide field-of-view using pixel super-resolution," Optics Express Vol. 18, Issue 11, pp. 11181-11191 doi:10.1364/OE.18.011181 (2010)

8. B. Khademhosseini, I. Sencan, G. Biener, T. Su, A.F. Coskun, D. Tseng, A. Ozcan, "Lensfree On-chip Imaging using Nano-structured Surfaces," Applied Physics Letters 96, 171106; doi:10.1063/1.3405719 (2010)

9. D. Tseng, O. Mudanyali, C. Oztoprak, S.O. Isikman, I. Sencan, O. Yaglidere and A. Ozcan, "Lensfree Microscopy on a Cell-phone" Lab on a Chip DOI:10.1039/c003477k (2010) Cover Article

10. O. Mudanyali, D. Tseng, C. Oh, S.O. Isikman, I. Sencan, W. Bishara, C. Oztoprak, S. Seo, B. Khademhosseini, and A. Ozcan, "Compact, Light-weight and Cost-effective Microscope based on Lensless Incoherent Holography for Telemedicine Applications" Lab on a Chip, DOI:10.1039/C000453G (2010)

11. G.Stybayeva, O. Mudanyali, S. Seo, J. Silangcruz, M. Macal, E. Ramanculov, S. Dandekar, A. Erlinger, A. Ozcan, A. Revzin, "Lensfree Holographic Imaging of Antibody Microarrays for High-Throughput Detection of Leukocyte Numbers and Function," Analytical Chemistry DOI: 10.1021/ac100142a (2010)

12. S.O. Isikman, I. Sencan, O. Mudanyali, W. Bishara, C. Oztoprak and A. Ozcan, "Color and Monochrome Lensless On-chip Imaging of Caenorhabditis Elegans Over a Wide Field-of-View" Lab on a Chip, DOI:10.1039/C001200A (2010)

13. C. Oh, S. O. Isikman, B. Khademhosseini and A. Ozcan, "On-chip differential interference contrast microscopy using lensless digital holography," Optics Express, Vol. 18 Issue 5, 4717-4726 doi:10.1364/OE.18.004717 (2010)

14. A.F. Coskun, T. Su, and A. Ozcan, "Wide field-of-view lens-free fluorescent imaging on a chip" Lab on a Chip, DOI: 10.1039=b926561a (2010)

Number of Papers published in peer-reviewed journals: 14.00

(b) Papers published in non-peer-reviewed journals or in conference proceedings (N/A for none)

None

Number of Papers published in non peer-reviewed journals: 0.00

(c) Presentations

1. A. Ozcan, “Lab-on-a-Cellphone as an Emerging Telemedicine Platform,” University of California, Global Health Day, UCI Campus 30 November 2010, Irvine CA

2. A. Ozcan, “Lensfree Imaging for Microscopy and Diagnostics,” First Look LA Meeting, USC Campus 16 November 2010, Los Angeles CA

3. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” UC Irvine Biomedical Engineering Department Seminar Series, 12 November 2010, Irvine CA

4. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” mHealth Summit, 9 November 2010, Washington DC

5. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Los Angeles IDEA Project, 7 November 2010, Los Angeles

6. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” LAUNCH: Health Forum, NASA Kennedy Space Center, 31 October 2010, Orlando

7. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Future Trends Conference, 18 October 2010, Miami, Florida

8. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Body Computing Conference, University of Southern California, 23 September 2010, Los Angeles, CA

9. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Google, 10 September 2010, Mountain View, CA

10. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Cisco, 2 August 2010, Milpitas, CA

11. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems,” Google-Nature-O’Reilly Science Foo Camp’10, Google Headquarters, 1 August 2010, Mountain View, CA

12. A. Ozcan, “Telemedicine Microscopy toward Smart Global Health Systems” National Geographic Explorers Symposium, 9 June 2010, Washington DC

13. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” Frontiers in Photonics Seminar Series, University of California, Irvine, 14 May 2010, Irvine CA

14. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” Photonics Seminar Series, University of Southern California (USC), 28 April 2010, Los Angeles CA

15. A. Ozcan, “Incoherent Lensfree Cell Holography for Global Health Applications” 7th International Conference on Optics-Photonics Design and Fabrication, (April 19-21 2010) Yokohoma, Japan

16. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” Optical Society of Southern California Monthly Meeting, 13 April 2010, Los Angeles CA

17. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” Stanford University Electrical Engineering Department, 12 April 2010, Stanford CA

18. A. Ozcan, “Lensless digital holography for telemedicine” SPIE Defense, Security, and Sensing Conference, Photonic Microdevices/Microstructures for Sensing, (April 5-9 2010) Orlando, USA

19. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” UC Berkeley EECS Department, 12 March 2010, Berkeley CA

20. A. Ozcan, “Photonics based Telemedicine Technologies toward Smart Global Health Systems” Stanford University Electrical Engineering Department, 11 December 2009, Stanford CA

21. A. Ozcan, Panelist at Vodafone Americas Foundation's Wireless Innovations Project Workshop, University of California, San Francisco, 10 December 2009, San Francisco CA

22. A. Ozcan, “Imaging of Cell Shadows for Global Health and Telemedicine Applications,” The Council of Scientific Society Presidents, Annual Meeting, 6 December 2009, Washington, DC

23. A. Ozcan, “Imaging of Cell Shadows for Global Health and Telemedicine Applications,” PopTech 2009 Conference, 23 October 2009, Camden, ME

24. A. Ozcan, “Lensfree On-Chip Imaging for Telemedicine Applications” 2009 CMOS Emerging Technologies Workshop, Vancouver, Canada

25. A. Ozcan, “A new tool for TeleMedicine: High-throughput On Chip Cytometry and Diagnostics,” MIT Media Labs, 22 September 2009, Cambridge, MA

26. A. Ozcan, “A new tool for TeleMedicine: High-throughput On Chip Cytometry and Diagnostics,” Vodafone Ventures Conference, 10 September 2009, London, UK

27. A. Ozcan, “Lensfree On-Chip Imaging for Telemedicine Applications” IEEE Photonics Society, 2009 Optical MEMS and NanoPhotonics Conference, (August 17-20, 2009) Florida

Number of Presentations: 27.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

None

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts): 0

Peer-Reviewed Conference Proceeding publications (other than abstracts):

1. W. Bishara, T. Su, A.F. Coskun, A. Ozcan, “High-resolution lensfree on-chip imaging over a wide field-of-view using source-shifted pixel superresolution,” SPIE Photonics West, Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing XVIII, January 2011, San Francisco, CA, paper # 7904-42

2. S.O. Isikman, C. Oh, D.K. Tseng, O. Mudanyali, A. Ozcan, “A compact and light-weight differential interference contrast (DIC) microscope for telemedicine applications,” SPIE Photonics West, Advanced Biomedical and Clinical Diagnostic Systems IX, January 2011, San Francisco, CA, paper # 7890-5

3. I. Sencan, A. F. Coskun, B. Khademhosseinieh, T. Su, G. Biener, and A. Ozcan, "Compressive decoding for incoherent lensfree on-chip imaging," SPIE Photonics West, Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing XVIII, January 2011, San Francisco, CA, paper # 7904-45

4. T. Su, A. Erlinger, D. Tseng, and A. Ozcan, ” Automated On-Chip Semen Analysis using a Handheld Lensfree Holographic Microscope”, SPIE Photonics West, Optical Diagnostics and Sensing XI: Toward Point-of-Care Diagnostics, January 2011, San Francisco, CA, paper # 7906A-5

5. O. Mudanyali, D. Tseng, S. O. Isikman, C. Oztoprak, I. Sencan, W. Bishara, O. Yaglidere, and A. Ozcan, “Lensfree Telemedicine Microscopy for Global Health Challenges”, SPIE/ Photonics West, Design and Quality for Biomedical Technologies IV, January 2011, San Francisco, CA, paper # 7891-18

6. O. Mudanyali, C. Oztoprak, D. Tseng, A. Erlinger, and A. Ozcan, “Field-Portable Lensfree On-Chip Microscopy for Detection of Waterborne Parasites”, SPIE/ Photonics West, Frontiers in Biological Detection: From Nanosensors to Systems, January 2011, San Francisco, CA, paper # 7888-13

7. B. Khademhosseinieh, I. Sencan, G. Biener, T. Su, A.F. Coskun, D. Tseng, and A. Ozcan, “Incoherent lensfree imaging on a chip using compressive decoding of nanostructured surfaces,” SPIE Photonics West, Nanoscale Imaging, Sensing, and Actuation for Biomedical Applications VII, January 2011, San Francisco, CA, paper # 7908-21

8. A.F. Coskun, I. Sencan, T. Su, and A. Ozcan, “Ultra-wide-field lensfree fluorescent imaging of caenorhabditis elegans on a chip,” SPIE Photonics West, Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues IX, January 2011, San Francisco, CA, paper # 7902-42

9. S.O. Isikman, S. Seo, I. Sencan, O. Mudanyali, T. Su, W. Bishara, A. Erlinger, A. Ozcan, “High-throughput Blood Analysis On a Chip using Lensless Digital Holography,” MicroTAS 2010 - The 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences, October 3-7, 2010, Groningen, The Netherlands

10. O. Mudanyali, C. Oztoprak, D. Tseng, A. Erlinger, A. Ozcan, “Water Quality Management using a Cost-effective and Field-portable Lensfree On-Chip Microscope,” MicroTAS 2010 - The 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences, October 3-7, 2010, Groningen, The Netherlands

11. D. Tseng, O. Mudanyali, C. Oztoprak, S.O. Isikman, I. Sencan, O. Yaglidere and A. Ozcan, “Lensfree Telemedicine Microscope on a Wireless Phone,” MicroTAS 2010 - The 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences, October 3-7, 2010, Groningen, The Netherlands

12. T. Su, S.O Isikman, W. Bishara, D. Tseng, A. Erlinger, and A. Ozcan, “Multi-angle lensfree holographic imaging for 3D cytometry on a chip,” ASME 5th Frontiers in Biomedical Devices Conference, September 20-21, 2010, Newport Beach, CA

13. A.F. Coskun, T. Su, and A. Ozcan, “Lensless on-chip fluorescent imaging over an ultra wide field-of-view,” ASME 5th Frontiers in Biomedical Devices Conference, September 20-21, 2010, Newport Beach, CA

14. S.O. Isikman, I. Sencan, O. Mudanyali, W. Bishara, C. Oztoprak and A. Ozcan, “Lensfree Color and Monochrome On-chip Imaging of Caenorhabditis Elegans Over a Wide Field-of-View,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

15. T-W. Su, D. Tseng and A. Ozcan, “Lensless on-chip microscope as a portable semen analysis device,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

16. B. Khademhosseini, I. Sencan, G. Biener, T. Su, A.F. Coskun, D. Tseng, A. Ozcan, “Lensfree Incoherent Microscopy on Nano-Structured Chips,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

17. W. Bishara, T-W Su, A.F. Coskun, and A. Ozcan, “High-resolution lensfree on-chip microscopy for wide-field imaging,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

18. O. Mudanyali, D. Tseng, S.O. Isikman, I. Sencan, W. Bishara, C. Oztoprak, S. Seo, B. Khademhosseini, and A. Ozcan, “Compact and Light-weight Telemedicine Microscope based on Lensfree On-Chip Imaging,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

19. C. Oh, S.O. Isikman, M. Lee and A. Ozcan, “Lensfree differential interference contrast (DIC) microscopy on a chip,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

20. A.F. Coskun, I. Sencan, T. Su, and A. Ozcan, “Ultra high-throughput lensfree fluorescent imaging using compressive sampling,” BMES Annual Meeting, October 6-9 2010, Austin Texas USA

21. S.O. Isikman, I. Sencan, O. Mudanyali, W. Bishara, C. Oztoprak and A. Ozcan, “Lensfree Color and Monochrome On-chip Imaging of Caenorhabditis Elegans Over a Wide Field-of-View” Bionano Systems Symposium UKC, August 11-15, 2010, Seattle, WA USA

22. S. Seo, T. Su, A. Erlinger, and A. Ozcan, “Red blood cell analysis using holographic LUCAS technique” Bionano Systems Symposium UKC, August 11-15, 2010, Seattle, WA USA

23. W. Bishara, T. Su, A.F. Coskun, and A. Ozcan, “Wide-field Lensfree On-Chip Microscopy using Pixel Super-Resolution,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

24. B. Khademhosseini, I. Sencan, G. Biener, T. Su, A.F. Coskun, D. Tseng, A. Ozcan, “Nano-structured surfaces for lensless incoherent microscopy on a chip” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

25. O. Mudanyali, D. Tseng, S.O. Isikman, I. Sencan, W. Bishara, C. Oztoprak, S. Seo, B. Khademhosseini, and A. Ozcan, “Light-weight, Field-portable and Cost-effective Lensfree Microscopy for Telemedicine Applications,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

26. S.O. Isikman, I. Sencan, O. Mudanyali, W. Bishara, C. Oztoprak and A. Ozcan, “High-throughput Lensless Imaging of Caenorhabditis Elegans on a Chip,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

27. A.F. Coskun, T. Su, and A. Ozcan, “Lensfree Fluorescent Imaging and Cytometry on a Chip,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

28. T. Su, S.O. Isikman, W. Bishara, D. Tseng, A. Erlinger and A. Ozcan, “Three-Dimensional On-Chip Cytometry by Multi-angle Lensless Holographic Imaging,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

29. I. Sencan, T.Su, A.F. Coskun and A. Ozcan, “Compressive sampling for ultra high-throughput lensfree on-chip fluorescent imaging,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

30. G. Stybayeva, O. Mudanyali, S. Seo, J. Silangcruz, M. Macal, E. Ramanculov, S. Dandekar, A. Erlinger, A. Ozcan, and A. Revzin, “Lensfree Holographic Imaging of Antibody Microarrays for High-Throughput Detection of Leukocyte Numbers and Function,” 11th Annual UC Systemwide Bioengineering Symposium, June 17-19, 2010, University of California, Davis, USA

31. C. Oh, S.O. Isikman and A. Ozcan, “Lensfree Polarization Microscopy On a Chip Using Incoherent Digital Holography,” OSA Conference on Lasers and Electro-optics (CLEO ’10) (May 16-21, 2010), San Francisco USA

32. S.O. Isikman, I. Sencan, O. Mudanyali, W. Bishara, C. Oztoprak and A. Ozcan, “Wide Field-of-View Lensless Imaging of Caenorhabditis Elegans On a Chip,” OSA Conference on Lasers and Electro-optics (CLEO ’10) (May 16-21, 2010), San Francisco USA

33. A. Ozcan, “Incoherent Lensfree Cell Holography for Global Health Applications” 7th International Conference on Optics-Photonics Design and Fabrication, (April 19-21 2010) Yokohoma, Japan (Invited Talk)

34. A. Ozcan, “Lensless digital holography for telemedicine” SPIE Defense, Security, and Sensing Conference, Photonic Microdevices/Microstructures for Sensing, (April 5-9 2010) Orlando, USA (Invited Talk)

35. T. Su, S. O. Isikman, W. Bishara, D. Tseng, A. Erlinger, and A. Ozcan, "Multi-angle Lensless Holography for Depth Resolved High-throughput Imaging of Cells On a Chip," IEEE Photonics Society, Winter Topical Meeting on Advanced Imaging in Bio-Photonics, (January 11-13 2010) Majorca, Spain

36. S. Isikman, S. Seo, I. Sencan, D. Tseng, O. Mudanyali, T. Su, A. Erlinger, and A. Ozcan, "Incoherent On-chip Cell Holography for Sub-cellular Imaging and Point-of-Care Diagnostics," SPIE Photonics West Conference, Imaging, Manipulation, & Analysis of Biomolecules, Cells, and Tissues VIII, January 2010, San Francisco, CA, paper # 7568-86

37. S. Isikman, S. Seo, Ikbal Sencan, A. Erlinger, and A. Ozcan, "Lensfree Cell Holography On a Chip: From Holographic Cell Signatures to Microscopic Reconstruction," IEEE Photonics Society Annual Fall Meeting (October 4-8, 2009) Antalya, Turkey

38. A. Ozcan, "Lensfree On-Chip Imaging for Telemedicine Applications" IEEE Photonics Society, 2009 Optical MEMS and NanoPhotonics Conference, (August 17-20, 2009) Florida (Invited Talk)

39. A. Ozcan, "Lensfree On-Chip Imaging for Telemedicine Applications" 2009 CMOS Emerging Technologies Workshop, Vancouver, Canada (Invited Talk)

40. A. Ozcan, "Lensfree On-Chip Imaging for Telemedicine Applications" Engineering Conferences International, Advances in Optics for Biotechnology, Medicine and Surgery XI, Clinical Challenges and Research Solutions, Burlington, Vermont, 2009 (Invited Talk)

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts): 40

(d) Manuscripts

None

Number of Manuscripts: 0.00

Patents Submitted

None

Patents Awarded

None

Awards

- LAUNCH Health Innovation Award, presented by NASA, USAID, Department of State, and NIKE, 2010
- Bill & Melinda Gates Foundation, Grand Challenges Explorations Award, 2010
- National Geographic Emerging Explorer Award, 2010
- Popular Mechanics Breakthrough Award, 2010
- Netexplorateur Award, Netexplorateur Observatory and Forum, France, 2010
- PopTech Science and Public Leaders Fellowship, 2010
- University of Southern California - Body Computing Slam Prize, 2010
- NIH Director's New Innovator Award, 2009
- Vodafone Americas Foundation - Wireless Innovation Award, 2009
- MIT's Technology Review Magazine, TR 35 Award, 2009
- IEEE Photonics Society Young Investigator Award, 2009

Graduate Students

NAME	PERCENT_SUPPORTED
Serhan Isikman	0.50
FTE Equivalent:	**0.50**
Total Number:	**1**

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
Waheb Bishara	1.00
FTE Equivalent:	**1.00**
Total Number:	**1**

Names of Faculty Supported

NAME	PERCENT_SUPPORTED	National Academy Member
Aydogan Ozcan	0.50	No
FTE Equivalent:	**0.50**	
Total Number:	**1**	

Names of Under Graduate students supported

NAME	PERCENT_SUPPORTED
Randy Lau	0.00
Anthony Erlinger	0.00
Pavan Datta	0.00
FTE Equivalent:	**0.00**
Total Number:	**3**

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period:	2.00
The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:	2.00
The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:	1.00
Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):	1.00
Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:	0.00
The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense	1.00
The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields:	0.00

Names of Personnel receiving masters degrees

NAME
Total Number:

Names of personnel receiving PHDs

NAME
Total Number:

Names of other research staff

NAME	PERCENT SUPPORTED
FTE Equivalent:	
Total Number:	

Sub Contractors (DD882)

Inventions (DD882)

Final Report for 56556-MS-DRP (PI: Aydogan Ozcan, UCLA)

(1) BAA Number: DARPA-BAA-09-31

(2) Technical Area: Photonics (*DSO: LtCol John Lowell, Ph.D.*)

(3) Lead Organization Submitting Proposal: University of California, Los Angeles

(4) Type of Business: "OTHER EDUCATIONAL"

(5) Other Team Members (if applicable) and Type of Business for Each: NONE

(6) Proposal Title: Lensless Imaging for Battlefield On-Chip Blood Diagnostics

(7) Technical Point of Contact to include: Prof. Ozcan, Aydogan, Engineering IV Building, Electrical Engineering, UCLA, Los Angeles, CA, 90095, Phone # 310 500 6568, Email: ozcan@ucla.edu;

(8) Administrative Point of Contact to include: Zhu, Julia, 11000 Kinross Avenue, Suite 102 Box 951406, Los Angeles, CA 90095-1406, Phone # (310) 794-0155, Email: JZhu@research.ucla.edu;

(9) Total Funds received from DARPA: 200,000 USD

(10) Duration (in months) of Proposed Work: 12 months

Statement of the Problem Studied and our Related Achievements

The needs and the requirements of medical diagnostics in resource limited settings such as the battlefield are significantly different than advanced medical laboratories. On the battlefield, medical resources, as well as trained personnel capable of running advanced diagnostic devices are difficult to find. Meanwhile, there is a growing need for cost-effective, compact, light-weight, and high performance diagnostic devices, equipped with advanced technologies, that can be used with minimally trained personnel to accurately analyze various bodily fluids such as blood, urine, saliva, sputum, sweat, etc. Analysis of these samples for diagnostic and sensing purposes requires a high-throughput platform that can specifically and accurately identify the characteristic signatures of target cells, bacteria or other bio-markers among thousands to millions of other micro- to nano-scale objects.

To provide a solution to these problems, within this proposal timeline (1 Year total) we developed a new lensless on-chip imaging platform, termed LUCAS, to enable both diagnostic and sensing capabilities within a cost-effective hand-held unit that is specifically suitable for the battlefield settings. We established the proof of concepts of this imaging modality to achieve reliable and repeatable quantified whole blood analysis and compared our results against commercially available blood analyzers. Furthermore, we investigated the fundamental limits on the size of the detectable cell/bacteria with this platform. These accomplishments resulted in several refereed journal and conference articles. This research effort included one postdoctoral scholar as well as one graduate student working under the leadership of the PI.

Summary of our Achievements on Lensfree Holographic Imaging and Blood Analysis on a Chip:

Lenses for several decades have been helping detectors (analog or digital) to operate at the *lowest possible space-bandwidth product* that is determined by the desired FOV and the resolution of the image. However, the recent digital revolution, driven mostly by consumer electronics market, has already advanced the state of the art for digital imagers such that a 2D space-bandwidth product of >10-20 Million is readily available nowadays. This implies that today's detector arrays are now much better suited to handle the *information distortion* caused by diffraction, which may then raise questions on the absolute necessity of the use of lenses in optical imaging. Moreover, today's digital processors (such as GPUs) together with novel algorithms are also in much better shape to process, *almost instantaneously*, the acquired information at the detector end for taking the job of a *physical lens*. Therefore, ***we can conclude that the widespread use of lenses (or similar wavefront shaping elements) in optical imaging can now be replaced for several application needs by cost-effective, compact and much simpler optical architectures that compensate in the digital domain for the lack of complexity of optical components.***

The fruits of this thinking have already appeared in the literature, where various lensfree on-chip imaging architectures were successfully demonstrated.[1-20] Among these approaches, lensfree digital holography deserves a special attention since with new computational algorithms and mathematical models,[21] it has the potential to make the most out of this digital revolution. *For this end, as part of this funding, our group has recently led the way to a new incoherent holography platform termed* ***LUCAS*** *(Lensless Ultra-wide-field Cell monitoring Array platform based on Shadow imaging).*[7-20]

LUCAS is fundamentally different from existing holographic approaches since it does ***not*** require a spatially or temporally coherent source. Instead, it works with an incoherent source (e.g., an LED) that is emanating from an unusually large aperture (e.g., 0.1mm). The key to the design of LUCAS is to realize that light waves pick up partial spatial coherence as they propagate, which implies that just over a few centimeters of free-space propagation they can effectively behave like a perfect coherent source for holographic imaging of micro-objects.[10] In its unique hologram recording geometry (see e.g., Fig. 1), LUCAS detects the ***holographic shadow*** signatures of the objects with unit magnification, which are then processed to enable digital recognition and microscopic imaging of the objects, achieving ~1-1.5 μm resolution over >20 fold larger FOV when compared to a conventional microscope objective-lens of similar resolution.[7,10]

There are several aspects of this LUCAS platform that makes it transformative for imaging and detection applications in especially field settings.

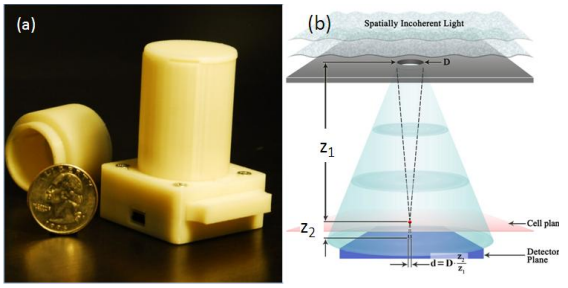

Fig. 1 (a) A LUCAS based lensless holographic microscope that weighs ~***45 grams*** (<1.6 ounces) is shown. It utilizes a simple LED source (at 591 nm) with an aperture of ~50-100 μm in front of the source. The LED and the sensor are powered through USB connection from the side. This lensfree holographic microscope claims the entire active area of the sensor as its imaging field-of-view (FOV ~ 24 mm^2), which constitutes >20 fold increase when compared to the FOV of a typical 10X objective-lens having a similar resolution. (b) Schematics of the holographic LUCAS microscope shown in (a). The target objects within the sample volume interact with the illumination light through *scattering, absorption and refraction* processes. This interaction then creates the holographic shadows of the objects on the digital sensor array, which contain their "*fingerprints*", permitting digital recognition and microscopic image reconstruction within <1 sec. Drawing not to scale. Typical values: z_1~2-4cm, z_2<1-2mm, D~50-100 μm.

First, the light source in this holographic approach does ***not*** need to be a laser such that a spatially incoherent source like a simple LED can be used. This feature greatly simplifies the optical set-up, making it cost-effective and compact, as well as digitally cleaning the object holograms by eliminating the coherent speckle noise and substrate induced multiple-reflection effects (see Figs. 1-3).[7,10] ***Second,*** this on-chip holography approach is not hungry for spatial coherence and therefore does not require a small aperture size for illumination which improves the light throughput of the imaging system by ***orders-of-magnitude*** without causing an issue for hologram pattern analysis or digital image reconstruction. This large aperture size (e.g., 50-100 μm - Fig. 1) also makes it robust to mechanical misalignments or potential clogging problems permitting a long time of operation without imaging artifacts or the need for realignment. ***Third***, because of its unit magnification (which is compensated entirely in the digital domain to achieve sub-pixel resolution), we can image a much larger field-of-view, typically by >20-100 fold than a conventional optical microscope (see e.g., Figs. 3-4). ***Fourth***, apart from reconstructing microscopic images of objects through holographic processing, we can also detect a unique 2D holographic texture (i.e., *a* ***fingerprint***) corresponding to each object, which provides an alternative source of digital information that complements the reconstructed object images. Through pattern/texture analysis of such holographic object signatures (both phase and amplitude) it is possible to recognize the type and the state of each object of interest without digital reconstruction [17,20], which is especially important for automated high-throughput detection/analysis applications.

This is an entirely new direction in lensfree holography which treats the amplitude and the phase of object holograms as fingerprints rather than data to be reconstructed. A major advantage of such an approach is that correlations calculated in the hologram domain are more sensitive than the image plane, especially for micro-scale

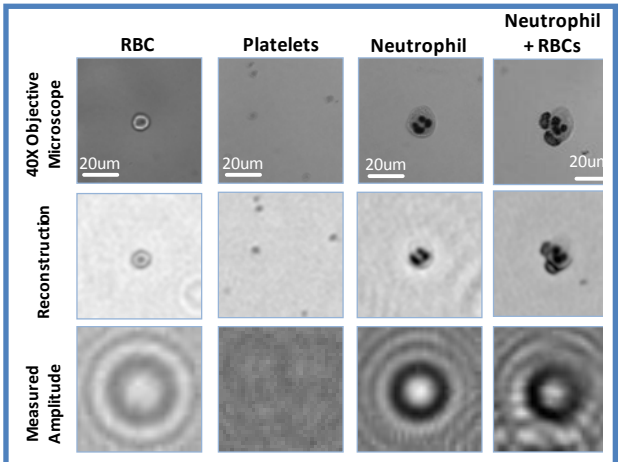

Fig. 2 Various blood cells imaged using the LUCAS holographic microscope of Fig. 1(a) are illustrated and compared against 40X objective-lens (NA=0.6) images of the same FOV. The bottom row illustrates the lensfree cell shadows (i.e., holograms) that are digitally processed (within < 10 ms) to reconstruct the middle row microscopic images of the samples. This reconstruction process can be achieved all in parallel across an FOV of ~24 mm^2 or even larger (e.g., ~18 cm^2) as shown in Fig. 3.

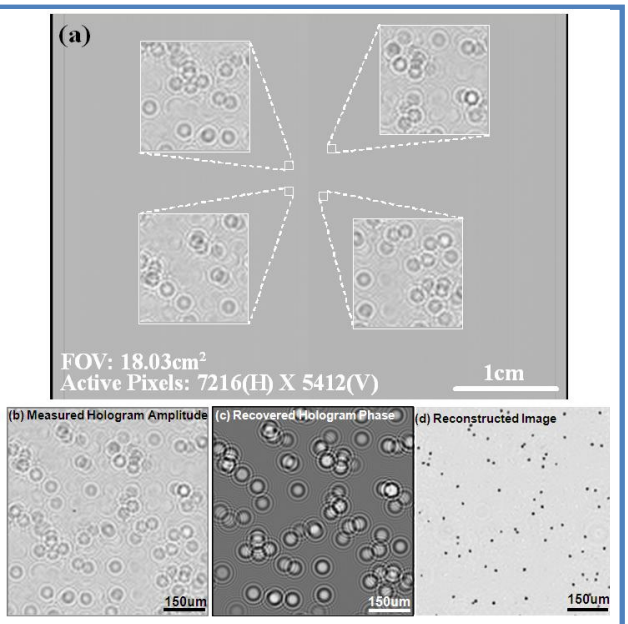

Fig. 3 Ultra-wide field-of-view (FOV) imaging of blood cells (over **~18 cm^2**) using a benchtop LUCAS platform is illustrated.[17] This constitutes ***~1000 fold larger FOV*** when compared to an optical microscope, permitting a throughput of >10 Million cells/second. (b) illustrates a digitally cropped region of interest taken from (a). (c) and (d) illustrate the recovered hologram phase and the reconstructed image of the cells, respectively. Each cell hologram and its corresponding phase exhibit oscillations that act as the "fingerprint" of the cell that can be used to assess the health of each cell individually.

objects that are imaged with a unit-magnification lensfree system. This important feature of lensfree holographic imaging enabled us to achieve sub-pixel resolution of ~1.4μm with unit-magnification using a pixel size of ~2.2μm over an FOV of ~24mm^2,[10,13] which would have been ***theoretically impossible*** for any *lens-based* system. Therefore, correlations and transformations occurring in the hologram domain exhibit several advantages toward high-throughput detection/analysis of target objects with significantly improved space-bandwidth products**.**

In addition to these, our group has also hit several other major milestones using the LUCAS platform. In particular, we achieved ***lensfree on-chip fluorescent imaging*** of labeled cells and particles over an ultra-wide FOV of ***>8 cm^2*** [16,18] as well as differential interference contrast (DIC) imaging,[10,13] i.e., Nomarski phase contrast microscopy, within the same LUCAS platform (see Fig. 4). Furthermore, we succeeded in detection of various bacteria such as *E. Coli* or *Giardia lamblia*, [14] as well as imaging of blood cells including platelets, monocytes, granulocytes, lymphocytes, and red blood cells.[10,17] Beyond wide-field microscopy, the LUCAS platform also enabled automated high-throughput cytometry by counting red and white blood cells with an accuracy of <5%, each, as well as quantification of the ***hemoglobin content*** of whole blood within the same lensfree platform.[17]

Furthermore, we have also we combined lensless holographic imaging with antibody microarrays for rapid and multiparametric analysis of whole blood samples on the same chip.[11] For this purpose, monoclonal antibodies specific for leukocyte surface antigens (CD4 and CD8, both of which are especially important for immunity assesment) and cytokines were printed in an array so as to juxtapose cell capture and cytokine detection antibody spots. Lensfree holographic on-chip imaging was then used to rapidly enumerate CD4 and CD8 T-lymphocytes captured on antibody spots and to quantify the cytokine signal emanating from IL-2, TNF-α and IFN-γ spots on the same chip.[11]

And finally, we also demonstrated, for the first time, the use of nano-structured surfaces [8] for lensfree on-chip microscopy to further improve the resolution. In this nano-structured on-chip imaging modality, the object of interest is directly positioned onto a nano-structured thin

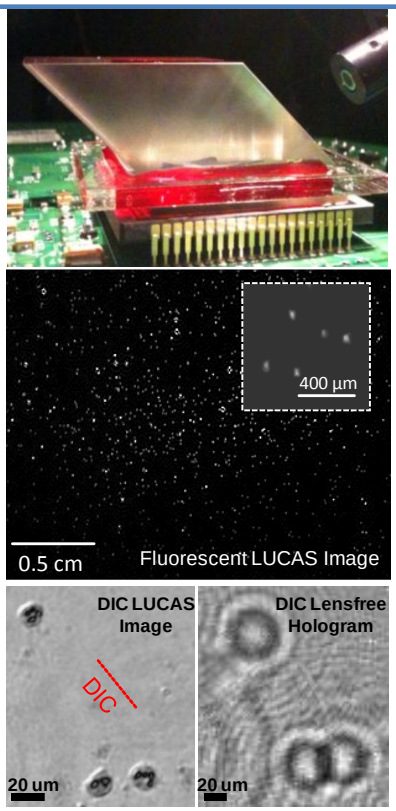

Fig.4 (*Top*) Ultra-wide field of view (FOV) lensfree on-chip fluorescent imaging set-up. (*Middle*) High throughput lensfree fluorescent imaging on a chip is illustrated over an *FOV of **8.4 cm^2*** for fluorescently labeled cells.[16,18] This lensfree fluorescent image was pumped through an LED and was acquired within an integration time of ~1 sec. The inset image is digitally cropped from the large FOV. The raw lensfree fluorescent images are digitally processed through compressive sampling to achieve a spatial resolution of ~10μm over >8 cm^2.[16] Dual imaging mode is also demonstrated to enable lensfree transmission holographic imaging and fluorescent imaging of an ultra-wide FOV within the same benchtop LUCAS platform.[18] (*Bottom Row*) LUCAS based DIC (Nomarski) images of white blood cells are demonstrated. The same holographic microscope of Fig. 1(a) can be converted into a lensless DIC microscope with two polarizers and thin birefringent crystals (e.g., quartz).[10,13] Each birefringent uniaxial crystal creates an ordinary and an extra-ordinary hologram of the cell, which are separated by a shear distance of ~1 μm from each other. The interference of these holograms codes the DIC information into the cell shadow.[13] Despite the major differences in the way that the lensless holograms are physically created and recorded for regular transmission imaging vs. DIC imaging, the image reconstruction process remains the same in both.[10,13] The shear direction is indicated in the figure with the red dashed line.

metallic film, where the emitted light from the object plane, after being modulated by the nano-structures, diffracts over a short distance to be sampled by a detector-array without the use of any lenses. The main function of the nano-structured surface is to encode the spatial resolution information into far-field diffraction patterns that are recorded in a lensfree configuration. This spatial encoding process is calibrated after the fabrication of the nano-structured surface, by scanning a tightly focused beam on the surface of the chip. For spatially incoherent imaging (e.g., for fluorescent objects on the chip) these calibration frames provide a basis which permits spatial expansion of any object distribution as a linear combination of these calibration images. Fortunately, calibration of a given structured chip has to be done only once, and ***any*** arbitrary incoherent object can be imaged thereafter using the same set of calibration images. Through a ***compressive sampling*** algorithm,[8,16] we decoded this embedded spatial information and demonstrated decomposition of a lensfree diffraction pattern into microscopic image of an incoherent object located on the chip with a sub-pixel spatial resolution of ~2μm. This imaging modality based on nano-structured substrates would especially be useful to create high-resolution lensfree fluorescent microscopes on a compact chip that could be used for specific imaging of labeled blood cells in resource poor settings.

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